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TITLE: FY08 DRMRP Clinical Trial: Strengthening Pathways to PTSD Recovery Using Systems-Level Intervention

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CONTRACTING ORGANIZATION: Research Triangle Institute
Research Triangle Park, NC 27709

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14. ABSTRACT

Over the course of the last year, the study team received IRB approval and began recruiting participants from the remaining study site, Ft. Bragg, and continued recruitment at the other five study sites (Joint Base Lewis-McChord, Ft. Bliss, Ft. Campbell, Ft. Carson, and Ft. Stewart). As of August 31, 2013, 1,320 total referrals across the six sites had been received; 666 participants had been enrolled and randomized into the study (332 participants into the STEPS UP arm; 334 participants into the optimized usual care arm); 556 participants completed the 3-month follow-up assessment; 418 participants completed the 6-month follow-up; and 181 participants completed the 12-month follow-up. At the end of June 2013 we stopped recruitment at five sites (JBLM, Ft. Bliss, Ft. Carson, Ft. Stewart, and Ft. Bragg), and stopped recruitment at Ft. Campbell at the end of July 2013. Multiple amendments have been approved by the WRNMMC IRB, including allowing for reimbursement for trial participation and offering multiple methods for collecting follow-up data. The study intervention has been refined; we continue site personnel training and coaching in the intervention and study procedures as well.

15. SUBJECT TERMS

PTSD; depression; preference-based stepped care; recruitment, enrollment/randomization, and follow-up; intervention refinement; hiring; training; IRB compliance

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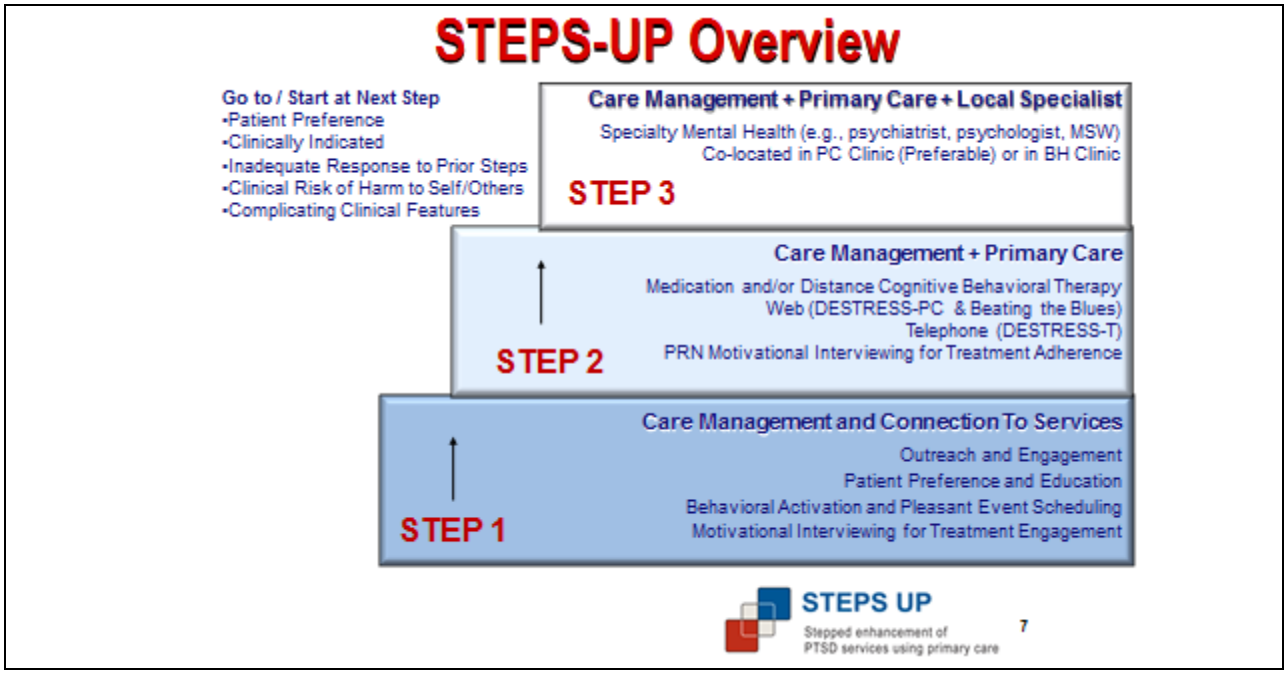
INTRODUCTION:

The purpose of the STEPS UP (**ST**epped **E**nhancement of **P**TSD **S**ervices **U**sing **P**rimary Care) trial is to compare centralized telephonic care management with preference-based stepped PTSD and depression care to optimized usual care. We hypothesize that the STEPS UP intervention will lead to improvements in (1) PTSD and depression symptom severity (primary hypothesis); (2) anxiety and somatic symptom severity, alcohol use, mental health functioning, work functioning; and (3) costs and cost-effectiveness. We further hypothesize that qualitative data will show that (4) patients, their family members, and participating clinicians find that the STEPS UP intervention is an acceptable, effective, and satisfying approach to deliver and receive PTSD and depression care.

Exhibit 1. STEPS UP Overview



STEPS UP is a six-site, two–parallel arm randomized controlled effectiveness trial with quarterly follow-up for 12 months comparing centralized telephonic stepped-care management to optimized usual PTSD and depression care. In addition to the existing PTSD and depression treatment options, STEPS UP will include web-based cognitive behavioral self-management, telephone cognitive-behavioral therapy, continuous RN nurse care management, and computer-automated care management support. Both arms can refer patients for mental health specialty care as needed, preferred, and available. The study will use sites currently running RESPECT-Mil, the Initiating PI's existing military primary care–mental health services practice network, to access site health care leaders and potential study participants at the six study sites.

If effective, we expect that STEPS UP will increase the percentage of military personnel with unmet PTSD- and depression-related health care needs who get timely, effective, and efficient PTSD and depression care. Our real-world primary care effectiveness emphasis will prevent the Institute of Medicine's so-called "15-year science-to-service gap." If successful, STEPS UP

could roll out immediately, reinforcing and facilitating pathways to PTSD and depression recovery.

BODY:

Overall

The RTI IRB approved the master protocol, consent form, and related study materials. During the past year, the study team received final IRB approval and began recruiting participants at the sixth study site, Ft. Bragg (February 2013). The study team also continued recruiting participants at the other five study sites: Joint Base Lewis-McChord (JBLM), Ft. Bliss, Ft. Campbell, Ft. Carson, and Ft. Stewart.

Throughout Year 4, RTI engaged in a variety of administrative activities and tasks, including coordination with the larger STEPS UP team, as well as RTI-specific tasks. We have held weekly meetings with the full STEPS UP team and weekly calls with DHCC to discuss planning and to work out details of study logistics, such as coordination with RESPECT-Mil at installations and facilitation of site IRB approvals. We have also held internal (RTI-only) weekly meetings to ensure that efficient progress is being made toward the study's goals. .

Other activities that transpired during this reporting year included the :

DSMB

During the past year, the STEPS UP team held two meetings with the DSMB. The first meeting of the DSMB was held in November 2012, where Dr. John Freedy was elected as DSMB Chair, and the second meeting was held in April 2013. We continue correspondence with the DSMB as needed, and plan to hold the next DSMB meeting in January 2014.

Revised SOW

In June 2013, we revised the SOW, per a request by Dr. Irvin. Our partners at DHCC and RAND also submitted revised SOWs. The primary update to the SOW was a revision to our target enrollment counts and timeline based on those changes in sample size.

IRB

From September 2012 through August 2013, RTI submitted 10 amendments, 2 informational updates, 1 audit, and 1 continuing review. *Table 1* presents details of each amendment that was submitted to and approved by the RTI IRB during Year 4.

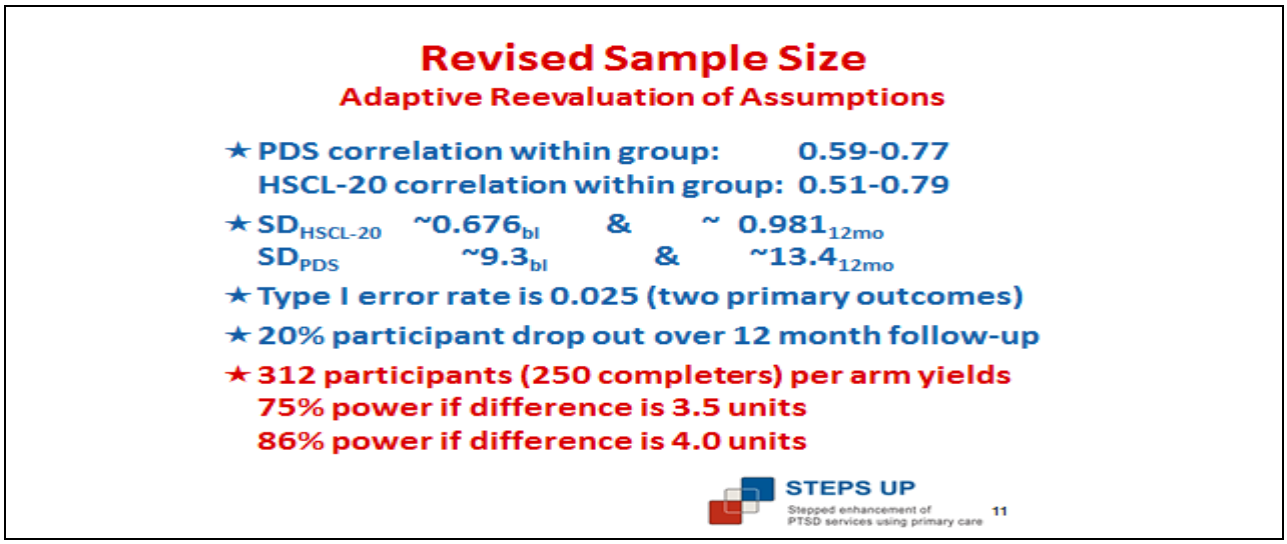
Table 1. Year 4 RTI IRB Amendments

Year 4 IRB Amendments	Highlight of Changes Requested and Approved
24 Sept 2012	Use of US Army LAN for self-administered web questionnaire.
29 Oct 2012	Review of revised consent forms to allow for incentives.
28 Nov 2012	Rescind the approval of a portion use of US Army LAN for self-administered web questionnaire.
3 Dec 2012	Distribution of retroactive incentives to study participants.
12 Dec 2012	Minor revisions to email text regarding distribution of retroactive incentives to study participants.
20 Dec 2012	Revisions to PAPI Lead Letter text.
23 Jan 2013	Minor revision regarding RTI transmission of participant contact information to RAND for qualitative study.
28 Jan 2013	Full audit (The project was reviewed for compliance with applicable regulatory requirements and standard operating procedures (SOPs).).
No approval required but it was submitted in March 2013	Site specific study materials for the RTI IRB records
29 April 2013	Continuing Review (renewal)
No approval required but it was submitted in May 2013	Updated site consent forms with new IRB expiration dates (all 05/07/2014) for RTI IRB records
23 May 2013	Minor revision regarding RTI transmission of participant contact information to RAND for qualitative study
28 Jun 2013	Allow batch tracing of participants using Social Security Number
30 Aug 2013	Allow electronic storage of consent forms

Revised Sample Size/Power Analysis

We examined the existing baseline data to determine variability in our main outcome measures, and conducted a power analysis based on these data. The results from this analysis showed that we would have adequate power for the study to test the main outcomes with approximately 625 enrolled participants. We presented this analysis to the DSMB and they concurred that this plan appeared to be adequate. The grant's Science Officer, Dr. Jordan Irvin, was informed of our plan to reduce the projected number of participants and stop enrollment at most sites at the end of June 2013. The study team opted to continue enrollment at Fort Campbell for an additional 4 weeks to ensure that the revised enrollment number of 625 was exceeded.

Exhibit 2. Revised Sample Size – April 2013



Web Instrument and Programming

In mid-October 2012, the RTI study team implemented A Case Management Control System for use by site coordinators and key RTI study staff..

Site Coordinators

In October 2012, the RTI study team hosted a 2 day training session in Research Triangle Park for the site coordinators, where in-depth training was provided on utilizing the new Case Management Control System. In addition, study protocol and best practices were reviewed and updated.

In January 2013, the STEPS UP Team, led by COL Charles Engel, conducted a series of site visits to all six study sites to discuss study progress with site personnel and local providers. The RTI staff researchers who manage the Site Coordinators traveled to the site visits at Ft. Bliss, Ft. Stewart, and Ft. Carson.

During this reporting year, all six sites were operational and staffed. Fort Bragg was our final site to begin enrollment, largely due to delays in IRB approval. Enrollment began at Fort Bragg in February 2013.

Data Collection

During Year 4, all six installations were recruiting and enrolling participants for baseline participation as well as follow ups. As of the end of August 2013, the study sites had received referrals for 1,320 Soldiers; 666 were enrolled in the study with 332 randomized to STEPS UP and 334 randomized to treatment as usual (TAU). There were 235 who weren't interested in the study and 419 ineligible.

Specific site information is described below. Exhibit 3 shows cumulative enrollment progress during the enrollment period.

Joint Base Lewis-McChord (JBLM): Baseline enrollments ended on July 22, 2013. As of the end of August 2013, 427 patients at JBLM had been referred to the study and 250 were enrolled. A total of 124 were randomized to STEPS UP and 126 to TAU. 82 weren't interested and 95 were ineligible.

- 3-month follow-up: at the end of August 2013, 245 participants had entered the 3-month follow-up window and 217 participants had completed their 3-month follow-up (109 STEPS UP, 108 TAU). Overall completion rate for this follow-up is currently 89%.
- 6-month follow-up: at the end of August 2013, 206 participants had entered the 6-month follow-up window and 176 participants had completed their 6-month follow-up (91 STEPS UP, 85 TAU). Overall completion rate for this follow-up is currently 85%
- 12-month follow-up: at the end of August 2013, 125 participants had entered the 12-month follow-up window and 97 participants had completed their 12-month follow-up (51 STEPS UP, 46 TAU). Overall completion rate for this follow-up is currently 78%.

Ft. Bliss: New baseline enrollments ended on July 15, 2013. At the end of August 2013, 283 patients had been referred to the study and 126 were enrolled. A total of 63 were randomized to STEPS UP and 63 to TAU. 56 weren't interested and 100 were ineligible.

- 3-month follow-up: at the end of August 2013, 125 participants had entered the 3-month follow-up window and 102 participants had completed their 3-month follow-up (55 STEPS UP, 47 TAU). Overall completion rate for this follow-up is currently 82%.
- 6-month follow-up: at the end of August 2013, 108 participants had entered the 6-month follow-up window and 81 participants had completed their 6-month follow-up (40 STEPS UP, 41 TAU). Overall completion rate for this follow-up is currently 75%.
- 12-month follow-up: at the end of August 2013, 52 participants had entered the 12-month follow-up window and 33 participants had completed their 12-month follow-up (18 STEPS UP, 15 TAU). Overall completion rate for this follow-up is currently 63%.

Ft. Campbell: New baseline enrollments ended during this quarter on August 31, 2013. At the end of August 2013, 423 patients had been referred to the study and 200 were enrolled. A total of 100 were randomized to STEPS UP and 100 to TAU. 60 weren't interested and 163 were ineligible.

- 3-month follow-up: at the end of August 2013, 170 participants had entered the 3-month follow-up window and 158 participants had completed their 3-month follow-up (74 STEPS UP, 84 TAU). Overall completion rate for this follow-up is currently 93%.
- 6-month follow-up: at the end of August 2013, 114 participants had entered the 6-month follow-up window and 104 participants had completed their 6-month follow-up (51 STEPS UP, 53 TAU). Overall completion rate for this follow-up is currently 91%.
- 12-month follow-up: at the end of August 2013, 50 participants had entered the 12-month follow-up window and 41 participants had completed their 12-month follow-up (19 STEPS UP, 22 TAU). Overall completion rate for this follow-up is currently 82%.

Ft. Carson: New baseline enrollments ended during this quarter on June 30, 2013. At the end of August 2013, 53 patients had been referred to the study and 18 were enrolled. A total of 9 were randomized to STEPS UP and 9 to TAU. 12 weren't interested and 24 were ineligible.

- 3-month follow-up: at the end of August 2013, 18 participants had entered the 3-month follow-up window and 17 participants had completed their 3-month follow-up (8 STEPS UP, 9 TAU). Overall completion rate for this follow-up is currently 94%.
- 6-month follow-up: at the end of August 2013, 16 participants had entered the 6-month follow-up window and 12 participants had completed their 6-month follow-up (4 STEPS UP, 8 TAU). Overall completion rate for this follow-up is currently 75%.
- 12-month follow-up: at the end of August 2013, 2 participants had entered the 12-month follow-up window and 1 participant had completed their 12-month follow-up (TAU). Overall completion rate for this follow-up is currently 50%.

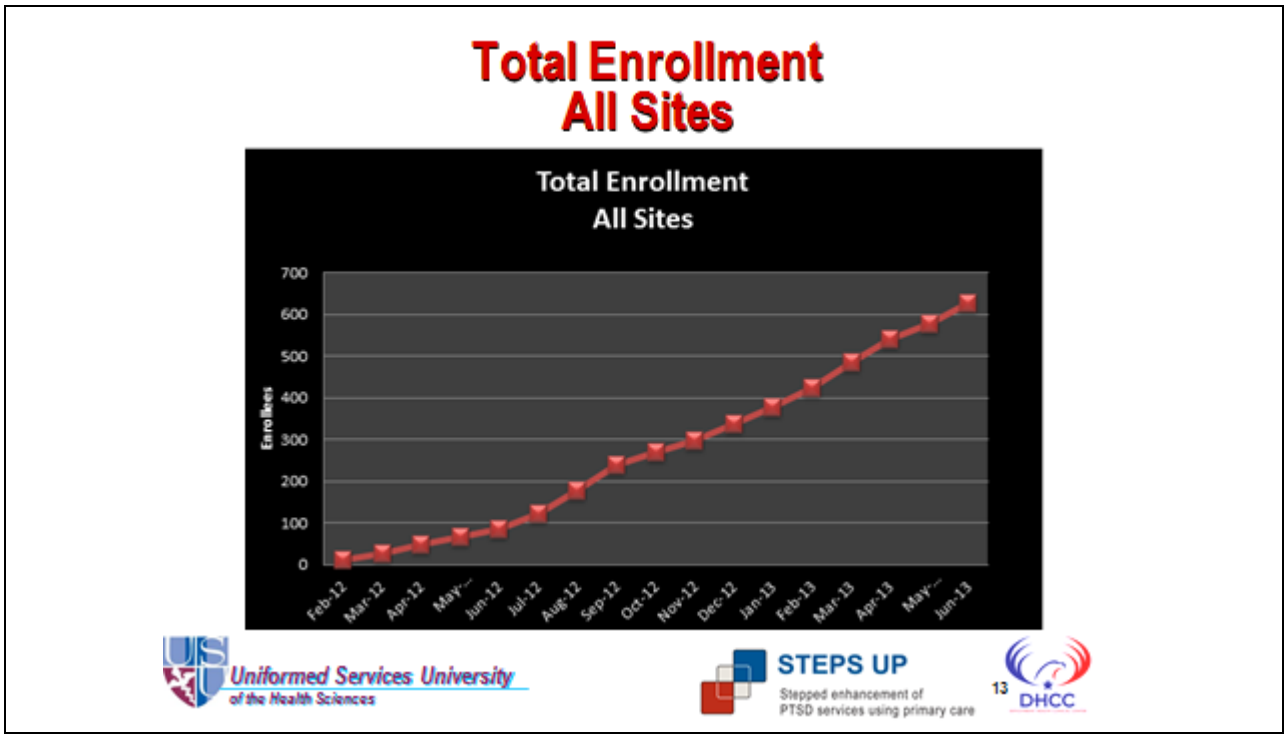
Ft. Stewart: New baseline enrollments ended during this quarter on July 15, 2013. At the end of August 2013, 82 patients had been referred to the study and 46 were enrolled. A total of 23 were randomized to STEPS UP and 23 to TAU. 8 weren't interested and 28 were ineligible.

- 3-month follow-up: at the end of August 2013, 46 participants had entered the 3-month follow-up window and 46 participants had completed their 3-month follow-up (23 STEPS UP, 23 TAU). Overall completion rate for this follow-up is currently 100%.
- 6-month follow-up: at the end of August 2013, 40 participants had entered the 6-month follow-up window and 37 participants had completed their 6-month follow-up (17 STEPS UP, 20 TAU). Overall completion rate for this follow-up is currently 93%.
- 12-month follow-up: at the end of August 2013, 10 participants had entered the 12-month follow-up window and 9 participants had completed their 12-month follow-up (4 STEPS UP, 5 TAU). Overall completion rate for this follow-up is currently 90%.

Ft. Bragg: New baseline enrollments ended during this quarter on July 15, 2013. At the end of August 2013, 52 patients had been referred to the study and 26 were enrolled. A total of 13 were randomized to STEPS UP and 13 to TAU. 17 weren't interested and 9 were ineligible.

- 3-month follow-up: at the end of August 2013, 24 participants had entered the 3-month follow-up window and 16 participants had completed their 3-month follow-up (10 STEPS UP, 6 TAU). Overall completion rate for this follow-up is currently 67%.
- 6-month follow-up: at the end of August 2013, 9 participants had entered the 6-month follow-up window and 8 participants had completed their 6-month follow-up (5 STEPS UP, 3 TAU). Overall completion rate for this follow-up is currently 89%.
- 12-month follow-up: at the end of August 2013, there were 0 participants in the 12-month follow-up window.

Exhibit 3. Total Enrollment All Sites



In an effort to increase follow-up rates, the study team has implemented the following measures:

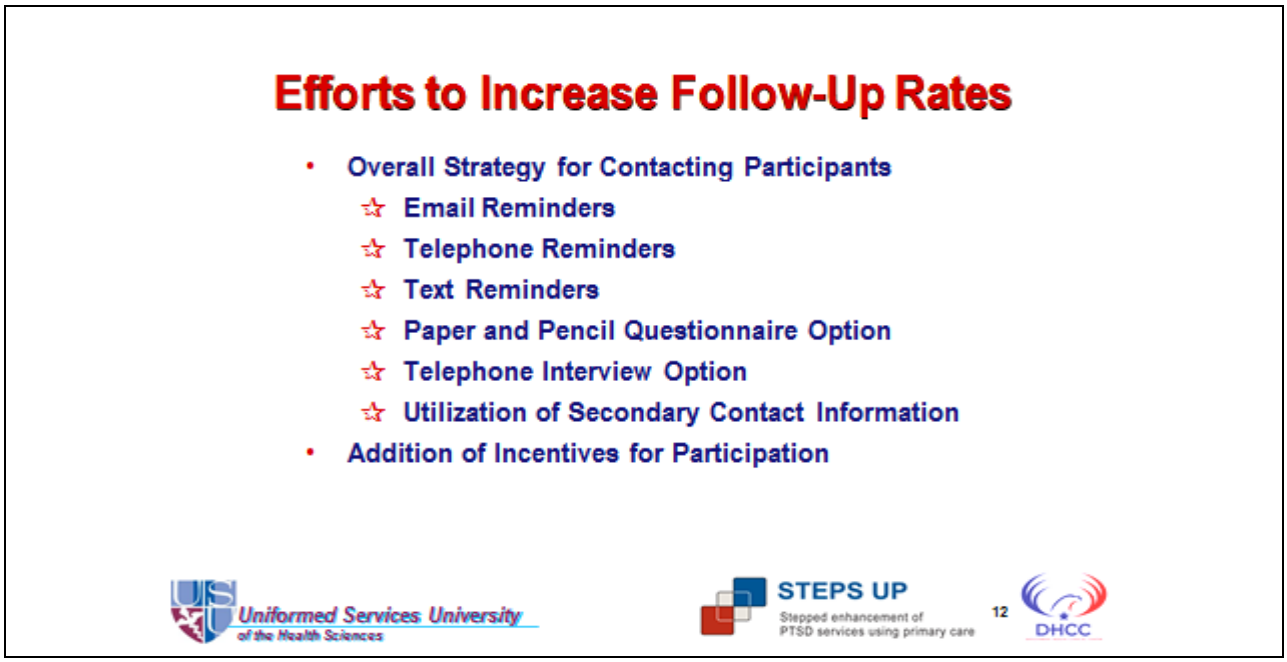
Telephone Interviews

In September 2012, RTI began conducting telephone interviews for participants who were due for a follow-up assessment. As of 31 August 2013, we had completed 70 telephone interviews. In many cases, when the telephone interviewer contacted participants, they elected to schedule an appointment with the site coordinator to complete their follow-up assessment in person rather than doing it by telephone.

Paper and Pencil Questionnaire (PAPI)

In January 2013, RTI began distributing paper and pencil (PAPI) questionnaires to participants as an option for them to complete their follow up assessments. As of 31 August 2013, we had received 5 completed PAPI questionnaires.

Exhibit 4. Follow Up Strategies



Qualitative Study

Throughout the reporting year, RTI submitted selected participant contact information, via an encrypted file every two weeks, to RAND for potential participation in the qualitative portion of the study. The qualitative recruitment goal was reached by RAND on 31 July 2013 and no further information was sent to RAND subsequent to this date.

Recruitment and Reimbursement for Participation

As is the case in all clinical trials and longitudinal studies, recruitment and retention are a full time concern. The predominantly young, male and highly mobile military demographic profile is a key issue. Our experience accomplishing controlled trials in this population has been an asset, and we have aggressively sought innovative recruitment and retention strategies. During this past year, we began distributing reimbursement for study participation in the form of Amazon.com gift cards.

Enrollment Errors

In October 2012, we uncovered programming issues with the survey that resulted in some misclassification of cases within the project. During the quarter from December 2012 to February 2013, we consulted with the IRBs and DSMB over specific plans for informing participants and for data analysis. The DSMB, RAND, RTI and WRNMMC IRBs have concurred with our proposed plan. At this time, we believe the issues are fully resolved, but continue to implement checking procedures to ensure there are not any additional errors. In March 2013, the WRNMMC IRB approved an amendment to cease the manual checks of the study web portal automated eligibility determinations, and continue a weekly automated check of

all eligibility determinations. To date, 706 soldiers have been screened for study eligibility from October 10, 2012 – August 23, 2013 and no errors were found based on our eligibility checks.

KEY RESEARCH ACCOMPLISHMENTS:

There are not yet any clear scientific findings resulting from this research as we are still in the data collection phase. Results are expected in June 2015.

REPORTABLE OUTCOMES:

The following presentation has been accepted for the Annual International Society for Traumatic Stress Studies (ISTSS) Meeting in November 2013 in Philadelphia, PA:

Engel CC, Freed MC, Lane B, Jaycox L, Bray R, Zatzick D, Litz B. (November 2013) DoD STEPS-UP: Design, Roll-Out and Early Lessons from a Randomized Effectiveness Trial of Collaborative PTSD Care in Army Primary Care. Part of ISTSS Symposium: Interventions for PTSD in Primary Care Medical Settings: Implementation and Early Effectiveness Outcomes. Meredith L (chair) & Zatzick D (discussant). International Society for Traumatic Stress Studies (ISTSS) conference, Philadelphia, PA.

CONCLUSION:

There are no conclusions to report at this time, as we are still in the data collection phase.

REFERENCES:

None